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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER |
|---|
| WILSON, MICHAEL C |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1632 | |

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DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/913,392 | HAN ET AL. | |
| | Examiner | Art Unit | |
| | Michael C. Wilson | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4-11 and 13-26* is/are pending in the application.

4a) Of the above claim(s) *16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-11,13-15 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 2, 3 and 12 have been canceled. Claims 1, 4-11, 13-26 remain pending.

### *Election/Restrictions*

This application contains claims 16-25 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's arguments filed 1-20-04 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claims 1, 4-11, 13-15 and 26 are under consideration in the instant office action.

### *Priority*

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

The effective filing date of the claimed invention is 2-11-2000, the filing date of PCT/KR00/00104, because 1999-4860, filed in Korea on 2-11-1999, did not teach isolating EG cells as claimed.

Applicants state claim 1 and Example 1 of the priority document indicate that PGCs are prepared in the first step that inherently comprise EG cells. Applicants'

argument is not persuasive. Regrettably, the translation of 1999-4860 filed 2-11-99 cannot be found. However, the priority document must teach that which is essential to the invention. In this case, the priority document does not teach or suggest that the PGCs comprised EG cells. It is not readily apparent that applicants suspected that the method described would result in EG cells (i.e. capable of making a germline chimera upon being introduced into a recipient embryo).

***Claim Rejections - 35 USC § 112***

Because the metes and bounds of the claims are unclear (see 112/2nd below), the essential culture methods required to enable one of skill to perform the method claimed cannot be determined. It is noted that, for example, Ponce De Leon (1997, Revista Brasileira de Reproducao Animal, Vol. 21, pg 96-101) taught LIF, bFGF, IGF and SCF are required for long term culture of avian PGCs. If long-term culture is required to make EG cells from PGCs, then an enablement rejection may be required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-11, 13-15 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is new matter. The steps and limitations added do not have support in the specification. "mitotically active" feeder cells cannot be found. The range of stage 20-36 cannot be found. "preferentially obtaining" EG cells cannot be found. "avian EG cell characteristics" cannot be found. "form an embryoid body..." cannot be found. "capable of differentiating into various cell types" and producing any "chimera expressing the EG cell phenotype" in the absence of producing a germline chimera cannot be found. A generic chimera that is not a germline chimera is not described in the specification and does not have a disclosed use. The three new steps in the method are not supported in the specification. Please point to the three steps in the specification that correlate to the three new steps in the claim.

Claims 1-15 and 26 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 remains indefinite because the metes and bounds of the materials and steps are unclear. Steps a), b) and c) are virtually identical except that the feeder layer in b) is mitotically active. "Preferentially obtaining EG cell colonies" in step b) is the same as producing a cell population of PGCs containing EG cell colonies as in step a). It is unclear if step a) is being repeated in step b) and c) or if the feeder cells used in a) are different than those in step b) and c).

The metes and bounds of what applicants consider PGCs and EG cell colonies and EG cell lines is unclear. Applicants argue PGCs were not pluripotent, therefore EG

cells are distinguished from PGCs (pg 9, 1st ¶). Applicants' argument is not persuasive. Chang (1997, Cell Biol. International, Vol. 21, pg 495-499) and Pain (1996, Development, Vol. 122, pg 2339-2348) taught PGCs were pluripotent and were capable of making chimeric chickens. It is unclear if EG cells must have a different structure or function than PGCs. The specification states EG cells are derived from PGCs (pg 1, last sentence) but does not define and distinguish EG cells and PGCs. The distinction between PGCs and EG cells as claimed cannot be determined. It is unclear if the method is directed toward culturing PGCs that become EG cells or if a population of PGCs that contain EG cells are cultured so that EG cells are preferentially obtained.

The metes and bounds of a "differentiation inhibitory factor" (claim 1) cannot be determined. It is unclear which, if any of the factors described in the specification (SCF, bFGF, IL-11, or IGF-I), are "differentiation inhibitory factors". Applicants argue the metes and bounds can be found on pg 6, lines 11-16. applicants' argument is not persuasive. Pg 6, lines 11-16, describe exemplary cell growth factors and do not define the metes and bounds of differentiation inhibitory factors. Pg 6, lines 15-16, states representative "differentiation inhibitory factor" is LIF, but does not define the metes and bounds of other such factors.

The metes and bounds of "germinal ridge stroma cells" (claim 5) remain unclear for reasons of record. It cannot be determined if any stromal cells from the gonad are encompassed by the phrase because such cells arise from the germinal ridge. It cannot be determined if the stromal cells must be isolated from an embryo at a particular stage.

Therefore, it is unclear if the phrase limits the structure of the stromal cell or when the stromal cell is isolated.

Claim 9 remains indefinite for reasons of record because the metes and bounds of "units" of LIF is unclear. It cannot be determined by what standard the units are measured. Applicants' refer to "Appendix I, col. 1, "Performance Characteristics," but it is unclear to what this refers. The specification and the art at the time of filing did not define the standard "units" of LIF.

***Claim Rejections - 35 USC § 102***

The rejection of claims 1, 4-11, 13-15 and 26 under 35 U.S.C. 102(b) as being anticipated by Pain (1996, Development, Vol. 122, pg 2339-2348) has been withdrawn. The STO feeder cells used by Pain were not mitotically active because they were treated with mitomycin C (pg 2340, "Preparation of culture...") which inhibits DNA synthesis and mitosis.

The rejection regarding claims 1, 4-11, 13-15 and 26 under 35 U.S.C. 102(e) as being anticipated by Petitte (US Patent 5,340,740), Petitte (US Patent 5,656,479) or Petitte (US Patent 5,840,510) has been withdrawn because Petitte taught culturing all the cells from a stage X-XIV embryo and isolating PGCs ('740; col. 6, line 50, through col. 8, line 7; claim 1-9). Petitte did not teach isolating PGCs from an avian at a stage from 20-36 as newly claimed.

The rejection of claims 1 4-11, 13-15 and 26 under 35 U.S.C. 102(e) as being anticipated by Ponce de Leon (US Patent 6,156,569) has been withdrawn. Ponce de

Leon taught isolating PGCs isolated from cells of stage XIV embryos. Ponce de Leon did not teach isolating PGCs from an avian at a stage from 20-36 as newly claimed.

The rejection of claims 1-13 and 26 under 35 U.S.C. 102(b) as being anticipated by Ponce de Leon (WO 99/06534, 2-11-1999) has been withdrawn. Ponce de Leon taught isolating PGCs isolated from cells of stage XIV embryos. Ponce de Leon did not teach isolating PGCs from an avian at a stage from 20-36 as newly claimed.

Claims 1, 4-6, 8, 10, 11, 13-15 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by Allioli (1994, Devel. Biol., Vol. 165, pg 30-37) for reasons of record.

Allioli taught isolating the gonads of stage 27-28 chicken embryos and culturing the cells therein in media. The cells included PGCs and fibroblasts. The fibroblasts created a feeder layer in culture and are "germinal ridge stroma cells" as claimed because they are isolated from gonads. The cells cultured were pluripotent. The media contained steel factor, LIF and FGF (pg 31, col. 2; 34, col. 2, "gonadal cell culture"; pg 36, col. 1, 2nd ¶), which are cells growth factors and differentiation inhibitory factors. Allioli taught culturing the PGCs in the same medium until colonies formed (pg 34, col. 2, last full ¶). The fibroblasts are inherently "mitotically active" because they were not treated with mitomycin C. This is the method used to make the feeder cells described in the specification.

Applicants' argument regarding the media used by Allioli is moot. Allioli taught using LIF and FGF, which is all that is required.

Applicants' arguments regarding the distinction between EG and PGCs is moot. No such distinction can be made from the specification or the art at the time of filing. The PGCs of Allioli are not patentably distinct from the EG cells claimed. The PGCs of Allioli were isolated in the exact same manner as described in the specification, i.e. from the gonad of a stage 27 embryo (¶ bridging pg 8-9).

Claims 1, 4-11, 13-15 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chang (1995, Cell Biol. Internatl. Vol. 19. No. 2, pg 143-149).

Chang taught isolating stromal cells and PGCs from the genital ridge of day 5 (stage 27-28) chicken embryos. The cells were cultured in media containing 10% FBS, 10 ng/ml of IGF, 10 ng/ml FGF and 10 units/ml LIF (pg 144, col. 1). These cells inherently contain PGCs (pg 144, col. 1, ¶ 4; col. 2, 3 lines from the bottom; pg 146, Fig. 2, "PGCs derived from 5-day embryonic ridge in culture"). The PGCs of Chang are isolated from the gonad of an avian blastoderm and are pluripotent. The cell culture was maintained for at least 4 days (pg 14, col. 1, 3rd ¶, line 5).

Chang taught culturing the PGCs in the same medium until colonies formed (pg 145, col. 9 lines from the bottom). The PGCs were recovered and subcultured for a period of time, which is equivalent to recovering and subulturing the established cell line.

Applicants' arguments regarding the distinction between EG and PGCs are moot. No such distinction can be made from the specification or the art at the time of filing. The PGCs of Allioli are not patentably distinct from the EG cells claimed. The PGCs of

Chang were isolated in the exact same manner as described in the specification, i.e. from the gonad of a stage 27 embryo (¶ bridging pg 8-9).

Applicants argue the PGCs of Chang were isolated from the blood. Applicants' argument is not persuasive. While some cells isolated by Chang were isolated from the blood, Chang taught isolating cells from the area where the gonads are developing (the germinal ridge, GR)(pg 143, 2nd ¶, lines 7-8; pg 144, col. 1, lines 1-5).

Applicants argue the PGCs are not isolated from the gonad. Applicants' argument is not persuasive because Chang clearly states the GR has developing gonads (pg 143, 2nd ¶, lines 7-8).

Applicants argue PGCs were not cultured for 4 days with the stromal cells. Applicants' argument is not persuasive. The feeder layer derived from GR had PGCs and the feeder layer PGCs (isolated from the GR of a 5-day embryo) had to be distinguished from PGCs isolated from the blood 2 day embryos (¶ bridging pg 144-145).

Applicants' argument regarding stage 13-14 is unclear.

Claims 1, 4-11, 13-15 and 26 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chang (1997, Cell Biol. Internatl., Vol. 21, No. 8, pg 495-499) for reasons of record.

Chang taught isolating germinal ridge stromal cells from day 5 (stage 27-28) embryos. The cells were cultured for 5 days in media containing IGF, FGF and LIF with germinal ridge stromal feeder cells isolated from day 5 embryos to obtain gPGCs. The

gPGCs were injected into recipient embryos and provided germline transmission (pg 496, "Materials and Methods"; pg 497, Fig. 1, "Progeny of germline chimeric chickens"). The gPGCs were recovered and subcultured for a period of time which is equivalent to recovering and subulturing the established cell line "in the same medium as in step a)" in step c). The gPGCs of Chang were EG cells because they provided germline transmission and were isolated from the germinal ridge of day 5 embryos.

Applicants have not provided any specific arguments to this rejection.

Claims 1, 4-6, 8, 10, 11, 13-15 and 26 remain rejected under 35 U.S.C. 102(e) as being anticipated by Petitte (US Patent 6,333,192, filed 8-9-1999) for reasons of record.

The effective filing date of the claimed invention is 2-11-2000, the filing date of PCT/KR00/00104, because 1999-4860, filed in Korea on 2-11-1999, did not teach isolating EG cells as claimed.

Petitte taught isolating PGCs and stromal cells from the gonads of stage 27-30 embryos. The cells were cultured in DMEM (col. 9, line 24-37, lines 49-55; claim 1). Petitte does not teach the avian fibroblasts were removed prior to adding the cells to STO feeder cells. Therefore, the culture of Petitte maintained for 5 days also has an avian fibroblast feeder cell matrix as claimed. The STO feeder cells can be replaced with avian fibroblast feeder cells (col. 5, line 64). LIF, IGF, FGF and SCF can be added to the media (col. 6, line 39). Thus, Petitte anticipates the claims.

Applicants' argument regarding the effective filing date of the instant invention is not persuasive. The translation of priority document 1999-4860 cannot be found.

Furthermore, inherency cannot be relied upon to teach that which is essential to the invention, i.e. that EG cells were present in the culture described in 1999-4860.

Applicants argue the cells by Petitte are not established by long-term culture. Applicants' argument is not persuasive. The claims do not require "long-term culture."

Applicants argue Petitte did not teach obtaining pluripotent cells. Applicants' argument is not persuasive. The cells were primordial germ cells, expressed an embryonic cell phenotype, which referred to an undifferentiated cell (col. 4, lines 30-32).

## *Conclusion*

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

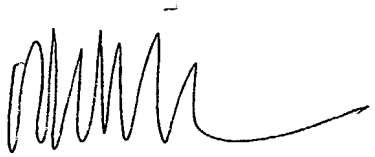
Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER